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09/937,060	04/15/2002	Olga Bandman	PF-0683 USN	4673

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Legal Department
Incyte Genomics
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EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/937,060	Applicant(s) Bandman et al.
	Examiner Rebecca Prouty	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 6, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above, claim(s) *1, 2, 7, 9, and 12-22* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *3-6, 8, 10, and 11* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's election with traverse of Group II(E), claims 3-6, 8, 10, and 11 as related to polynucleotides encoding SEQ ID NO:5 in Paper No. 10 is acknowledged. First it should be noted that contrary to applicants portrayal of the previous action as a restriction **and** an election of species, the previous action contained **only** a restriction between 168 distinct groups and no election of species. The construction of the action in two parts (Groups I-XII and A-N) was done only to conserve space in writing the groups and to make the restriction more easily understood. Applicants traverse on several grounds: (a) that under the PCT Administrative Instructions unity of invention exists between a polypeptide and claims to polynucleotides encoding those polypeptides; (b) that Groom et al. (EMBO J. 15(14): 3621-3632, which was cited in the international search report and thus previously provided to applicant but provided herein to be certain applicants have a copy) or Ruben et al. do not disclose a protein within Groups I(A)-I(N) and even assuming that this is the case that unity still exists between the other remaining polypeptides of Group I and the corresponding polynucleotides; (c) that claims 3-7 all depend from Claim 1 and have unity therewith because dependent claims (claims which share all features of the claim from which they depend and are in the same

category of invention) share unity of invention with the claim from which they depend under MPEP section 1850(A); and (d) all applicants claims recite corresponding technical features of the claimed polypeptide sequences of SEQ ID NO:1-14 and thus all form a single general inventive concept.

Each of applicants arguments is unpersuasive. Examiner acknowledges that the under the PCT Administrative Instructions unity of invention exists between a polypeptide and claims to polynucleotides encoding those polypeptides **when** the polypeptide is a special technical feature as defined under PCT Rule 13.2. However, the polypeptides of Groups I(A)-I(N) as claimed do **not** constitute a special technical feature under PCT Rule 13.2 because each of these groups include more than the specific polypeptides of SEQ ID NOS:1-14 but each includes polypeptides comprising any biologically active or immunologically active fragment of SEQ ID NOS:1-14. Such polypeptides have been found in the prior art such as in Groom et al. or Ruben et al. as the proteins of Groom et al. and Ruben et al. as well as all of SEQ ID NOS:1-14 all comprise the amino acid glutamine which is a biologically active compound. Furthermore the polypeptide of Group I(E) corresponding to elected Group II(E) is further not a special technical feature as defined under PCT Rule 13.2 as

Kohama et al. teach a sphingosine kinase which comprises a sequence identical to amino acids 77-109 of SEQ ID NO:5 as well as many other fragments of SEQ ID NO:5. Thus the polypeptide of Group I(E) lacks any corresponding special technical feature with the polynucleotides of the elected group. Furthermore, applicants arguments that MPEP section 1850(A) requires that Claims 3-7 have unity with Claim 1 because dependent claims share unity of invention with the claim from which they depend is misplaced. As is further explained in MPEP 1850, if an independent claim does not avoid the prior art, then the question whether there is still an inventive link between all the claims dependent on that claim needs to be carefully considered. If there is no link remaining, an objection of lack of unity may be raised. As has been previously explained the polypeptide sequence of Claim 1 does not constitute a special technical feature and thus there is no inventive link between Claims 1 or 7 and the claims of the elected group. Furthermore, it should be noted that Claim 3 is not even a dependent claim of Claim 1 within the meaning of MPEP 1850(A) as the polynucleotides of Claim 3 do not have all the features of the polypeptides of Claim 1. Polypeptides and polynucleotides are chemically different compounds.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 2, 7, 9, and 12-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in Paper No. 10.

Claims 3-6 and 8 are objected to as depending from a non-elected claim.

Claims 3-6, 8, and 10 are objected to as encompassing non-elected subject matter.

Claims 3-6, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (upon which Claims 3-6 and 8 depend) is indefinite in the recitation of "biologically active" as it is unclear what the scope of activities that is encompassed by this term includes. On page 12 of the specification, applicant's define the term "biologically active" as "having structural, regulatory or biochemical functions of a naturally occurring molecule". As the number of naturally occurring molecules is vast, and the scope of possible structural, regulatory or biochemical functions

is even broader with no clear boundaries of what these terms include, the scope of "biologically active fragments" of SEQ ID NO:5 is vague and indefinite.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-6, 8, 10 and 11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The applicant has asserted utility for the polypeptide of SEQ ID NO:5 encoded by the claimed isolated polynucleotide of SEQ ID NO:19 as a protein kinase or a protein phosphatase or for "diagnosis, treatment or prevention of neurological, cell proliferative and autoimmune/inflammatory disorders". However, the asserted utilities are not specific and substantial. While Table 2 states that the protein of SEQ ID NO:5 exhibits a diacylglycerol kinase catalytic domain "signature sequence", and thus the specification could be interpreted to assert that SEQ ID NO:5 is a kinase, the specification fails to assert what compounds the protein of SEQ ID NO:5 phosphorylates. Kinases comprise a highly diverse group of proteins which phosphorylate a

wide variety of different compounds including, proteins, carbohydrates, lipids and nucleic acids. Even if one interpreted the disclosure of Table 2 as asserting that SEQ ID NO:5 is a diacylglycerol kinase, (which assertion is not in fact made), the prior art discloses a protein with 82% identity to SEQ ID NO:5 which has sphingosine kinase activity but not diacylglycerol kinase activity (see Kohama et al., page 23726). This protein has substantially greater homology to the protein of SEQ ID NO:5 than any diacylglycerol kinase found in the prior art. The closest homolog having diacylglycerol kinase activity that can be found appears to be that of Ding et al. to which the protein of SEQ ID NO:5 has only 5% homology overall and 25% homology to the catalytic domain. As such a skilled artisan would not find an assertion that the protein of SEQ ID NO:5 is a diacylglycerol kinase reasonable without further supporting evidence. No such evidence is presented in the specification. As kinases are such a large diverse family of enzymes, a mere disclosure that a protein is a kinase without a more specific recitation of what type of kinase (i.e., what compound(s) is phosphorylated) is insufficient to provide a substantial utility as the skilled artisan would require further research to identify or reasonably confirm a real world context of use. The specification also lists a general use for the polypeptides encoded by the claimed

polynucleotides as useful for "diagnosis, treatment or prevention of neurological, cell proliferative and autoimmune/inflammatory disorders". However, there is no information that links the use of the polypeptide of SEQ ID NO:5 or the polynucleotide of SEQ ID NO:19 and its variants to any specific disease state. Thus the asserted utility of the claimed polynucleotides and its variants is not substantial or specific. Further, while the specification discloses that SEQ ID NO:19 and its fragments will be used to generate probes, that is not a utility specific to the claimed polynucleotide sequence. For all the reasons detailed above, the claimed polynucleotides lack, a specific, substantial and credible utility.

Claims 3-6, 8, 10, and 11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if applicants show that a polynucleotide encoding the protein of SEQ ID NO:5 has a patentable utility, the following scope of enablement rejection would still apply.

Claims 3, 5, 6, 8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being

enabling for polynucleotides encoding SEQ ID NO:5, does not reasonably provide enablement for polynucleotides encoding any naturally occurring protein which is 90% identical to SEQ ID NO:5, any biologically active fragment or immunologically active fragment of SEQ ID NO:5 or any DNA which is 90% identical to SEQ ID NO:19 or comprises a fragment of at least 60 nucleotides of SEQ ID NO:19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 3, 5, 6, 8, 10 and 11 are so broad as to encompass any polynucleotide encoding any naturally occurring protein which is 90% identical to SEQ ID NO:5, any biologically active fragment or immunologically active fragment of SEQ ID NO:5 or any DNA which is 90% identical to SEQ ID NO:19 or comprises a fragment of at least 60 nucleotides of SEQ ID NO:19. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which portions of a protein's amino acid sequence have any desired activity requires a knowledge of and guidance with regard to the ways in which the

proteins' structure relates to the desired function. However, in this case the disclosure is limited to the structure and function of SEQ ID NO:19 and its encoded polypeptide, SEQ ID NO:5.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any polynucleotide encoding any naturally occurring protein which is 90% identical to SEQ ID NO:5, any biologically active fragment or immunologically active fragment of SEQ ID NO:5 or any DNA which is 90% identical to SEQ ID NO:19 or comprises a fragment of at least 60 nucleotides of SEQ ID NO:19 because the specification does **not** establish (A) regions of the protein structure which may be modified without effecting

kinase activity; (B) the general tolerance of kinases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including DNA sequences encoding any naturally occurring protein which is 90% identical to SEQ ID NO:5, any biologically active fragment or immunologically active fragment of SEQ ID NO:5 or any DNA which is 90% identical to SEQ ID NO:19 or comprises a fragment of at least 60 nucleotides of SEQ ID NO:19. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 3, 5, 6, 8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of DNA molecules encoding any naturally occurring protein which is 90% identical to SEQ ID NO:5, any biologically active fragment or immunologically active fragment of SEQ ID NO:5 or any DNA which is 90% identical to SEQ ID NO:19 or comprises a fragment of at least 60 nucleotides of SEQ ID NO:19. The specification does not contain any disclosure of the function of all DNA sequences encoding any naturally occurring protein which is 90% identical to SEQ ID NO:5, any biologically active fragment or immunologically active fragment of SEQ ID NO:5 or any DNA which is 90% identical to SEQ ID NO:19 or comprises a fragment of at least 60 nucleotides of SEQ ID NO:19. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed

genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Accession No. AA639414.

GenBank Accession No. AA639414 discloses a polynucleotide identical to nucleotides 1141-1553 of SEQ ID NO:19 which would encode a fragment of SEQ ID NO:5 identical to amino acids 338-384. Therefore, GenBank Accession No. AA639414 anticipates claims 3 and 11.

Claims 3 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Accession No. AI042283.

GenBank Accession No. AI042283 discloses a polynucleotide identical to nucleotides 1115-1553 of SEQ ID NO:19 which would encode a fragment of SEQ ID NO:5 identical to amino acids 329-384. Therefore, GenBank Accession No. AI042283 anticipates claims 3 and 11.

Claims 3, 5, 6, 8, 10 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Young et al. (WO98/54963).

Young et al. discloses a polynucleotide (named gene 80 by Young et al.) 94% identical to SEQ ID NO:19, polynucleotides comprising a promoter operably linked thereto, host cells transformed therewith and the expression of the protein encoded. Therefore, Young et al. anticipates claims 3, 5, 6, 8, 10 and 11.

Claims 3, 5, 6, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Kohama et al.

Kohama et al. discloses a polynucleotide encoding mouse sphingosine kinase, polynucleotides comprising a promoter operably linked thereto, host cells transformed therewith and the expression of the protein encoded. The sphingosine kinase of Kohama et al. comprises a fragment identical to amino acids 77-109 of SEQ ID NO:5 as well as many other fragments of SEQ ID NO:5. Kohama et al. further teach fragments of a putative human

sphingosine kinase identical to many fragments of SEQ ID NO:5.

Therefore, Kohama et al. anticipates claims 3, 5, 6, and 8.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kohama et al. in view of GenBank Accession Nos. D31133, AA232791, W63556, AA081152, and AA026479.

Kohama et al. is discussed above. Kohama et al. further disclose that the putative human sphingosine kinase sequence was obtained by assembling sequences from several ESTs, i.e., from GenBank Accession Nos. D31133, AA232791, W63556, AA081152, and AA026479. However, Kohama et al. do not report the polynucleotide sequence which was obtained from the disclosed

assembly. Therefore, it would have been obvious to one of ordinary skill in the art to compare each of the human cDNAs of the ESTs to the mouse sphingosine kinase gene of Kohama et al. and to each other and to assemble the fragments into a full length polynucleotide encoding a human sphingosine kinase. This polynucleotide would clearly have greater than 90% identity to SEQ ID NO:19.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652